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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,444	02/10/2004	Bruce D. Cohen	PC25232A	2037

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EXAMINER	
DUFFY, BRADLEY	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,444	COHEN ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 20 ,2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,12 and 14-17* is/are pending in the application.

4a) Of the above claim(s) *2,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-8, 10, 12 and 16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of the instant application has changed here at the Patent and Trademark office. Please direct future inquiries concerning this application to Brad Duffy whose telephone number is (571) 272-9935.

2. The amendment filed May 20, 2008, is acknowledged and has been entered. Claim 1 has been amended. Claims 9, 11 and 13 have been canceled.

3. Claims 1-8, 10, 12 and 14-17 are pending in the application.

4. Claims 2, 14 and 15 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 24, 2007.

Notably, Applicant has further elected the following species of invention wherein the agent species is an "analgesic"; the vaccine species is an "autologous tumor vaccine"; the anti-proliferative agent species is a "PDGFR inhibitor"; the antibody species is "2.13.2"; the VH gene species is "VH DP-47; and the VL gene species is "A30". Due to the Applicant's cancellation of claim 9, the VH and VL gene species election is currently moot.

5. Claims 1, 3-8, 10, 12 and 16-17 are under examination.

6. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

7. As set forth in the previous office action, the deposit of antibody 2.13.2 is not required, because the specification discloses the entire amino acid sequences of the light and heavy chain of antibody 2.13.2. Please see Figure 3.

Claim Objections

8. Claim 1, 3-8, 10 and 12 are objected to because the claims are drawn in the alternative to the subject matter of a non-elected invention or a non-elected species of invention.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In this case claim 12 is indefinite because the claim depends from cancelled claim 11. As such, the method now encompassed by this claim cannot be ascertained. Therefore, one of ordinary skill in the art would not be apprised of the metes and bounds of the subject matter that is regarded by Applicant as the invention, so as to permit the artisan to know or determine infringing subject matter.

Grounds of Rejection Withdrawn

11. Unless specifically reiterated below, Applicant's amendment and/or arguments filed May 20, 2008, have obviated or rendered moot the grounds of rejection set forth in the previous Office action mailed February 20, 2008.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. The rejection of claim 17 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** a method of treating multiple myeloma in a mammal comprising administering to said mammal the anti-IGF-1R antibody 2.13.2 comprising a heavy chain polypeptide comprising the amino acid sequence of SEQ ID NO: 45 and a light chain polypeptide comprising the amino acid sequence of SEQ ID NO: 47 in an amount effective to inhibit the progress of multiple myeloma, **does not reasonably provide enablement for using** a method of treatment or prevention of aging in a mammal comprising administering to said mammal an amount of an anti-IGF-1R antibody that is effective in treatment of prevention of aging, is maintained. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Again, there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

At page 6 of the response filed May 20, 2008, Applicant has submitted that this rejection has been overcome by the amendment to claim 1 which has deleted the reference to "prevention".

In response, while Applicant's amendments and submissions have been carefully considered, because Applicant does not address how the specification would enable one of skill in the art to treat or prevent aging by administering to a mammal an anti-IGF-1R antibody, this rejection has been maintained with respect to claim 17.

As evidenced by, Yu et al in the previous office action, many complex and diverse conditions are associated with aging and the specification does not provide enablement for treating or preventing these conditions. Furthermore, "aging" *per se*, occurs due to the passage of time, i.e., every day a mammal has "aged" one day more than the previous day, and the specification presents no evidence that "aging" *per se* could be treated or prevented. Therefore, one of skill in the art would be subject to undue and unreasonable experimentation to treat or prevent "aging" by administering to a mammal an anti-IGF-1R antibody.

Accordingly, it is maintained for these reasons and as set forth in the Office action mailed February 20, 2008, that the specification as filed does not enable methods of treating or preventing "aging". In this case, the amount of guidance, direction, and exemplification in the specification is not sufficient to reasonably enable the skilled artisan to treat or prevent "aging" by administering to a mammal an anti-IGF-1R antibody at the time the application was filed without undue and unreasonable experimentation.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. The rejection of claims 1, 3-8, 10 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsiades et al (of record) in view of Cohen et al (of record) and Masferrer (of record) and Carosella et al (of record), is maintained.

The claims are herein drawn to a method of treating multiple myeloma in a mammal comprising administering to said mammal a 2.13.2 anti-IGF-1R antibody in an amount effective to treat said multiple myeloma. The claims further comprise administering antibodies in combination with an analgesic agent such as ibuprofen, an anti-emetic agent such as granisetron hydrochloride, an anti-vascular agent such as bevacizumab and as anti-proliferative agent such as PDGFR inhibitors or autologous tumor vaccines. Furthermore, as detailed in the above rejection of claim 12 under 35 U.S.C. 112, second paragraph, because claim 12 depends form canceled claim 11, the method that Applicant intends to be encompassed by this claim cannot be determined

and therefore, it also cannot be determined if the prior art renders this claim obvious. For this reason, claim 12 is not being included in this rejection.

At page 6 of the amendment filed May 20, 2008, Applicant has traversed this ground of rejection.

Applicant has argued that a *prima facie* case of obviousness has not been made out because there was no motivation in the cited references directing one of ordinary skill to select the 2.13.2 antibody for treating multiple myeloma (MM). Applicant further argues that there are many different antibodies against IGF-1R receptor disclosed in Cohen et al and that there is nothing in Mitsiades et al, Cohen et al, Masferrer or Carosella et al that leads to the selection of the particular antibody 2.13.2 from the vast number of possible IGF-1R antibodies for treating MM.

In response, this argument is not found persuasive because contrary to Applicant's assertions, as explained in the previous office action, the combined teachings of Mitsiades et al and Cohen et al would have led one of skill in the art to select the 2.13.2 antibody of Cohen as an IGF-1R inhibitory antibody that is suitable for administering to patients for treating multiple myeloma. Notably, as set forth in the previous office action, Mitsiades et al teach that the IGF/IGF-1R system is a major therapeutic target for Multiple Myeloma (MM), and that an inhibitory anti-IGF-1R antibody suppressed the growth of MM patient tumor cells while Cohen et al teach that the antibody 2.13.2 is such an inhibitory anti-IGF-1R antibody that inhibits the binding between human IGF-1R and IGF-1. In further response, the teachings of Cohen et al would further motivate one of skill in the art for selecting the 2.13.2 antibody for treating MM because Cohen et al teach that the 2.13.2 antibody is one of two disclosed anti-IGF-1R antibody which reduces IGF-1R induced phosphotyrosine signals in tumor cells that express IGF-1R (see entire document, e.g., Figure 5 and description of figure 5 on page 6). For these reasons, one of skill in the art would have been motivated to select the inhibitory 2.13.2 anti-IGF-1R antibody of Cohen for administering to patients for treating MM because Mitsiades et al establish that inhibiting the IGF-1R pathway in MM tumor cells with an inhibitory anti-IGF-1R, inhibits the growth of MM tumor cells and

because Cohen et al establishes that the 2.13.2 antibody can inhibit the IGF-1R pathway. Therefore, one of skill in the art would also have had a reasonable expectation of success in treating MM by administering to MM patients the inhibitory 2.13.2 anti-IGF-1R antibody in view of these references. In this case, the 2.13.2 anti-IGF-1R antibody of Cohen is specifically identified as being able to inhibit the IGF-1R pathway, and for this reason, contrary to Applicant's allegations otherwise, one of skill in the art would have been motivated to select this particular antibody to treat MM in view of these references.

Accordingly, because the teachings of Mitsiades et al, Cohen et al, Masferrer and Carosella et al would have led one of skill in the art to treat MM patients by administering the 2.13.2 antibody alone or in combination with the other claimed agents, as set forth in the previous office action, it is maintained that the invention as a whole was obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

For these reasons and the reasons explained in the previous Office action, Applicant's argument that the rejection should be withdrawn is not persuasive and the rejection of Claims 1, 3-8, 10 and 16 under 35 U.S.C. 103(a) as being unpatentable over Mitsiades et al in view of Cohen et al and Masferrer and Carosella et al, is maintained.

17. The rejection of claims 1, 3-8 and 16 under 35 U.S.C. 103(a) as being unpatentable over Mitsiades et al (of record) in view of Emanuel et al (of record) and Masferrer (of record) and Carosella et al (of record), is maintained.

The claims are herein drawn to a method of treating multiple myeloma in a mammal comprising administering to said mammal an anti-IGF-1R antibody in an amount effective to treat said multiple myeloma. The claims further comprise administering antibodies in combination with an analgesic agent such as ibuprofen, an anti-emetic agent such as granisetron hydrochloride, an anti-vascular agent such as

bevacizumab and anti-proliferative agents such as PDGFR inhibitors or autologous tumor vaccines.

At pages 7 and 8 of the amendment filed May 20, 2008, Applicant has traversed this ground of rejection.

Applicant has argued that the claimed invention is drawn to the treatment of MM with antibody 2.13.2 and that these is no motivation in the cited references directing one of ordinary skill to select the 2.13.2 antibody for treating multiple myeloma (MM).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., antibody 2.13.2) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, Applicant's argument is not found persuasive because as explained in the previous office action, one of ordinary skill in the art would have been motivated and would have reasonable expectation of success in treating multiple myeloma in a mammal comprising administering an anti-IGF-1R antibody because Mitsiades et al teach that a neutralizing anti-IGF-1R antibody suppressed the growth of MM patient tumor cells and that blockage of IGF-1R with neutralizing anti-IGF-1R antibodies can be clinically applicable for patients with MM, and because Emanuel et al teach methods for treating cancers comprising administering a therapeutically effective amount of an antibody directed against the growth factor receptor associated with the cancer. Accordingly, because Mitsiades et al teach that IGF-1R is a growth factor receptor associated with the MM and because Mitsiades et al teach a neutralizing anti-IGF-1R antibody which suppresses the growth of MM patient tumor cells, one of skill In the art would have been motivated to administer such a neutralizing anti-IGF-1R antibody which suppresses the growth of MM tumor cells to MM patients by the methods of Emanuel et al. Furthermore, based on these teachings, one of skill in the art would have had a reasonable expectation of success in treating MM because the antibody of Mitsiades inhibits the IGF-1R pathway and the growth of MM cells expressing IGF-1R

and because Emanuel et al teach methods of administering antibodies to treat patients with a cancer associated with a growth factor receptor.

Accordingly, because the teachings of Mitsiades et al, Emanuel et al, Masferrer and Carosella et al would have led one of skill in the art to treat MM patients by administering a neutralizing anti-IGF-1R antibody alone or in combination with the other claimed agents, as set forth in the previous office action, it is maintained that the invention as a whole was obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

For these reasons and the reasons explained in the previous Office action, Applicant's argument that the rejection should be withdrawn is not persuasive and the rejection of Claims 1, 3-8 and 16 under 35 U.S.C. 103(a) as being unpatentable over Mitsiades et al in view of Emanuel et al and Masferrer and Carosella et al, is maintained.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
September 2, 2008